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MEDICAL LABORATORIES

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THE utilization of laboratory methods in the diagnosis of infectious diseases probably dates back to the time when the *Bacillus anthracis* was found to be the microbe causing anthrax in sheep and when Pasteur discovered the organism producing "pebrine" in the silkworm. In 1880, the protozoan causing malarial fever was identified in the blood and thereafter in rapid succession the bacteria inducing many other diseases were described. Methods for the isolation and study of the various disease-producing germs were developed to such an extent that the new science of bacteriology became established and subsequently expanded so greatly that few bacteriologists claim expert knowledge in the entire subject. As a result of the study of the action of pathogenic bacteria on the animal body, it was found that many organisms induce the formation of specific substances, the presence of which may be readily found in the blood. Two common illustrations of this phenomenon are typhoid fever and syphilis.

In all departments of science, what are primarily toys or curiosities soon become useful and necessary appliances in everyday life. This constitutes progress. The science of medicine in particular leaps forward with each new discovery or new method of procedure. Witness the germ theory of disease and its subsequent elaboration and proof; the far-reaching effects of the observation by Theobald Smith and Kilbourne that insects may act as the intermediate hosts in the transmission of disease; the value of prophylaxis, the perfection of the microscope, the invention of the stethoscope and the use of the aniline dyes in bacteriology and pathology. The story of the marvelous progress of medical science during the past fifty years is more interesting than anything hitherto published and yet the tale is but begun. The narration of medical progress is of extreme interest to the lay public and this is testified to by the avidity with which magazines and newspapers publish medical news in all detail. This interest should be encouraged and stimulated, for only with the active cooperation of the public can medicine accomplish its greatest triumph—the elimination of disease by preventive measures.

The hot-house of medical progress is the laboratory. Destroy the laboratory and we revert to the medical practice of the fifteenth century. The physician would again take up his individual method of guessing in which he is frequently justified by a kind nature which has limited the progress of most diseases. In the absence of animal experimentation the old "shot-gun" prescription would again come into vogue, and the unscientific and irrational use of a multitude of drugs would be the prevailing fashion. Since laboratory methods are often precise in the information which they yield and in many other instances give highly suggestive findings, it is logical to conclude that they should not be neglected even in apparently trivial cases. Experience may be extensive, knowledge deep and the special senses highly developed, but instruments and exact methods should be employed for confirmation if not for purposes of actual diagnosis. Information thus obtained is a source of great satisfaction because a permanent record is established, and the subsequent treatment justified.

Diagnosis of the disease present is essential because upon it depends not only the character of the treatment, but also the prognosis which frequently is of great importance and invariably most earnestly inquired about by the patient. While he may feel interested in knowing the name of his affliction, the sick person is more concerned regarding the ultimate outcome of his case. The value of prognosis is well illustrated by typhoid fever. This disease is caused by the *Bacillus typhosis* and the diagnosis may be established by finding the microbes in the blood during the first three or four days of the illness, or by subsequent examination of the blood by the Widal method and by counting the leucocytes. Typhoid fever is a "self-limited" disease and the mortality is usually 5-20 per cent., varying somewhat in different epidemics. Closely related to the typhoid bacillus is the paratyphoid bacillus, of which there are two strains. Infection by these organisms produces a train of symptoms similar to typhoid fever but more mild. Fatal cases are extremely rare and in paratyphoid fever the physician would have no hesitancy in predicting a favorable termination of the illness. The diagnosis between these conditions can only be established by laboratory methods.

In medical practise the physician finds many diseases the manifestations of which are so typical as to leave no doubt regarding the diagnosis. Thus scarlet fever, measles and small-pox are detected without great difficulty. There are many others, however, with variable signs and symptoms in different

individuals and it is in these cases that the laboratory plays so important a part. As a matter of interest, let us group the various diseases commonly found in this country according to their dependency for diagnosis on laboratory methods.

GROUP A

Diseases diagnosticated with certainty by laboratory methods

Typhoid fever	Leprosy
Syphilis	Tetanus
Diphtheria	Gaseous gangrene
Cholera	Diabetes
Cerebrospinal meningitis	Malaria
Gonorrhea	Intestinal parasites
Tuberculosis	Trichinosis
Actinomycosis	Anemia
Bacillary dysentery	Pernicious anemia
Amebic dysentery	Leukemia
Anthrax	Chlorosis
Pneumonia	Hemophilia
Glanders	Tumors

GROUP B

Diseases in which the diagnosis is greatly assisted by laboratory methods

Septicemia	Abscess
Nephritis	Appendicitis
Gout	Peritonitis
Lead poisoning	Asthma
Poliomyelitis	Erysipelas
Typhus fever	Influenza
Vincent's angina	Whooping-cough
Pneumonia	Smallpox
Meningitis	Tumors

The above list, although not very long, includes by far the greatest amount of morbidity ordinarily prevalent. Most diseases are due directly or indirectly to bacteria and the demonstration of the presence of the suspected pathogenic organisms usually suffices to establish the diagnosis. The exceptions are the few instances in which individuals normally harbor disease-producing bacteria. Such persons are termed "carriers" and the most frequent examples are those that harbor diphtheria bacilli in the throat or typhoid bacilli in the intestine or gall-bladder. In the army cantonments it has been shown conclusively that normal individuals act as carriers of virulent meningococci and pneumococci.

In recent years laboratory work has received great emphasis in medical education. Medical colleges are usually judged and

rated by the quality of their laboratory courses and consequently the young graduate of the present day considers, and rightfully so, that laboratory methods are essential to the successful practise of medicine. He regards the necessary apparatus as part of his armamentarium and, indeed, as important as the stethoscope or thermometer. Laboratory technique, however, is so time consuming that busy practitioners find it impossible to perform any but the simplest examinations and so turn to the nearest well-organized institution for assistance. While recent graduates maintain a proper viewpoint toward the diagnostic laboratory, the older practitioners are too often indifferent and unwilling in many instances to avail themselves of laboratory service. They are content with their clinical diagnosis and, while undoubtedly correct in most instances, yet they should confirm their estimate of the case by an exact method if available. In this way only can they successfully claim to be scientific practitioners of medicine.

When we speak of exact methods in diagnosis we usually mean an accuracy of 90-95 per cent. Because of the multitude of variable factors concerned and the changing conditions of the body, it is scarcely possible to attain greater accuracy. Usually in practice the chief reason for the failure to arrive at a correct diagnosis lies in the lack of thoroughness on the part of the physician or the omission of repeated tests and examinations. When one considers the complex human organism and the frequent variations in the course of disease it is scarcely to be expected that a given set of factors necessary to the diagnosis will remain constant through any great period of time. Thus by way of illustration is leukemia a progressively fatal disease in which, however, "remissions" occur, that is, periods, usually of brief duration, when the patient is practically normal so far as can be determined objectively. Of course, an examination made at such a time will yield negative results and yet a few days later decided and positive changes will occur. Again, in malaria, the blood when examined between chills may be negative, but shortly before the chill will be found to contain myriads of the specific organisms. In diabetes, no sugar or very little, may be found in the urine, but the blood, on examination, will be found to contain a greatly increased amount. Thus it will be seen that the intelligent application of laboratory methods is essential to success. Properly speaking, the medical laboratory should not and can not as a rule make a diagnosis. The laboratory worker reports his findings to the physician, who correlates the results with his clinical observations and

thus arrives at the true diagnosis. Medical laboratories are frequently termed diagnostic laboratories, but improperly so, for their function is to obtain additional data for the attending physician who is the only one qualified to make the diagnosis. Laboratories may occasionally be in error in their reports, either because of the natural fluctuations or complications of disease or because of incomplete observations, or more rarely error in technique. That "experience is fallacious and judgment difficult" is just as true to-day as in the time of Hippocrates, but the degree of error in diagnosis is constantly decreasing. The personal equation, however, is still an important factor in the work.

In every community where hospitals are situated, many surgical operations are performed during the year and tissues or organs removed from the body, but not always submitted to the pathologist for examination. All such specimens should be sent to the laboratory for microscopic study. Complete records, including stained sections of the tissue, should be made and kept permanently. Thus in later years, if necessary, it will be possible to examine these records in the light of new illnesses or symptoms that may arise. This is more frequently necessary than is commonly believed, particularly in the case of abdominal operations, where the removal of an appendix or ovary, for instance, is in question. Our best surgeons have such examinations made as a routine for several reasons, chiefly, however, as a matter of scientific interest and to confirm their pre-operative diagnosis.

That many physicians who are indifferent to the advantages offered by laboratory assistance can no longer remain so is becoming more evident with each succeeding year. The public is gradually acquiring a rather extensive knowledge of disease and the application of laboratory methods, and many patients now show a decided interest in the laboratory reports. This attitude should be encouraged because it will lead to greater cooperation on the part of the patient in treatment and preventive measures. During the present Great War the sanitary department of the army has acquired a position second to none in importance and the chief reliance of that organization is upon the laboratory. The increasing activity of state and municipal health departments who insist on laboratory examinations in suspected cases of tuberculosis, typhoid fever, poliomyelitis and meningitis is but one indication of the importance of the medical laboratory. The war has brought about a serious and earnest attempt to control venereal diseases. Registration of

infected individuals will undoubtedly soon be required in many states and the basis for the acts of the authorities will depend largely, if not entirely, on the laboratory examinations. When this war is over, millions of men will return to civil life impressed with the value of the laboratory in the diagnosis and prevention of disease. They will know that typhoid fever, pneumonia, meningitis and many other diseases are only properly diagnosed by the finding of the causative organism, that the rational treatment of wounds and other infections depends upon knowing the nature of the bacteria present, that the efficacy of the treatment for syphilis can be best judged by the Wassermann reaction and that the diagnosis of a host of other conditions requires special skill and training on the part of the physician. The doctor can no longer arbitrarily say to his patient that he has such or such ailment, but must in support of his diagnosis cite the laboratory report. This information not only helps the patient, but is also instructive to the physician.

Diagnosis, however, is only part of the work of the medical laboratory. No such institution is properly organized unless ample funds and facilities are available for research. While the efficiency of the laboratory may be kept at a high point in the performance of routine tests, the systematic investigation of new problems should be part of the daily labor. Research may be carried on to elucidate new facts, to confirm previous studies, to record isolated cases of scientific and practical interest, to improve existing methods, or to collect statistics for future study. This special investigation minimizes the dulling effect of routine and acts as a mental stimulus to the laboratory worker. Thus we find the best laboratories continually engaged in research and they who have thus acquired the experimental viewpoint are much more likely to explain an uncommon train of symptoms or determine the nature of a puzzling case.

What is the future of the medical laboratory? Although remarkably well developed at the present time, we find that, in view of the many great problems which medical science must yet solve, these institutions have only begun their work. The discovery of disease germs, yet to be made, new methods in the diagnosis and prevention of infections, and even improvement of existing methods, offer fields for many years of labor. Here and there isolated workers have contributed valuable facts and made important discoveries, but innumerable fundamental problems yet remain. Only recently the advent of new methods have led to morphologic studies of great importance, thus again opening a field which at one time was thought closed. The ex-

tensive subject of functional diseases is being clarified by the methods of chemical analysis now in use and the new science of colloidal chemistry will further aid greatly in the solution of many perplexing medical problems.

Hand in hand with the discovery of the cause of disease is the problem of therapy. In comparatively few instances can diseases be cured after they have become well established. Chief among these are diphtheria, malaria, hook-worm infection, syphilis and cerebro-spinal meningitis. There are a host of other diseases dependent upon functional derangement of various organs and their alleviation depends largely on hygienic and dietetic measures. Many other abnormalities are relieved usually by the removal of the offending organ and then nature reestablishes the normal state, with or without further assistance. Examples of these are appendicitis, goiter, calculi and tumors. Thus it is seen that the greatest practical progress made in medical science has been along lines of prevention. This has been accomplished primarily by isolation and the elimination of conditions favorable to the growth and transmission of microbes and secondly by preventive inoculation.

Consider for a moment how successfully malaria, yellow fever, plague and smallpox have been controlled. These diseases, in the past, decimated whole populations and at times threatened to destroy entire nations. Who can estimate the value to the world of the control of these four infections alone? The destruction of mosquitoes and rats, the method of vaccination, simple procedures and not at all difficult of application, have already been of immeasurable benefit to mankind. They all represent the work of the medical laboratory, except smallpox vaccination, which was made known to the world by Edward Jenner before the days of medical laboratories. Later day improvements in the production and use of vaccine were made, however, in the laboratory.

The two great objects of medical endeavor in recent years have been to prevent infection, either before or shortly after exposure, and to apply a specific remedy after the onset of symptoms. The success of Pasteur in preventive inoculation against anthrax in sheep led to the adoption of similar methods in many other infectious diseases with varying results. Having apparently exhausted all possibilities along these lines, the laboratory workers turned to chemistry and sought to obtain drugs or chemical products which when injected into the body destroyed the parasites, but without inducing harmful changes in the organs. The most brilliant results obtained have been by

the use of atoxyl in sleeping-sickness and salvarsan in syphilis. Thus it is seen that medical investigation has become an exceedingly complex subject and that the united efforts of the physician, the biologist, the chemist and the physicist are necessary in order to obtain favorable results. Physical science is rapidly looming to the front as an aid in the solution of medical problems and has already accomplished much, as in the application of our knowledge concerning the X-ray and radium in the treatment of disease.

The organization of a well-conducted medical laboratory calls for a competent staff and adequate equipment. The primary object is to render immediate and necessary service in the diagnosis and prevention of disease. This means that a certain amount of routine work will be conducted for the physicians and hospitals in the neighborhood. The second important object of the laboratory is to engage in research. This may be along lines to which the institution is committed, or will depend on the interests of those in charge of the laboratory, or upon accidental findings during the routine examinations. Much valuable work has been accomplished as a result of chance observations, but they really are not accidental, because the workers are ever on the lookout for unusual phenomena. Owing to the liberality of wealthy citizens of this country, many buildings have been erected and equipped for diagnostic and research purposes and they are sufficient for years to come. What is needed urgently is endowment for existing institutions and funds for salaries and materials to conduct research. Many laboratories well equipped as to working space and apparatus are unable to carry on investigations because of lack of finances. It is futile to erect buildings for scientific purposes unless funds are also provided for the work. With such support and encouragement the problem of the infectious diseases and tumors will soon be solved and their eradication is certain to follow. The greater portion of the remaining diseases will be cared for by the science of hygiene which is making such rapid progress.